Hemostasis management of tooth extraction in a patient with Bernard–Soulier syndrome and a severe bleeding tendency: A case report

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ABSTRACT

Bernard–Soulier syndrome is characterized by thrombocytopenia, giant platelets, and severe bleeding; although bleeding varies widely, it is usually evident from childhood and requires particular attention during surgeries. We extracted a fractured tooth and performed hemostasis management in a male patient with a Bernard–Soulier syndrome-related severe bleeding tendency after intracerebral hemorrhage. The preoperative platelet count was abnormally low (7×10^9/L). Normal coagulability was observed. After intravenous hydrocortisone administration, he received 10 human leukocyte antigen-matched platelet units. The extraction sites were packed with gelatine sponges and a splint was used for hemostasis. Excellent hemostasis was achieved with minimal human leukocyte antigen-matched platelets.

KEYWORDS

Bernard–Soulier syndrome
HLA-matched platelets
Optics method in fluorescent platelet channel
Bleeding tendency
Hemostasis management

INTRODUCTION

Bernard–Soulier Syndrome (BSS) is a very rare, autosomal-recessive inherited disorder characterized by thrombocytopenia, giant platelets, severe bleeding, and deficient ristocetin-induced platelet aggregation[1]. BSS occurs extremely rarely in European, North American, and Asian populations, which have been studied most intensively; a prevalence of <1/1000,000 has been estimated from the cases reported previously. In Japan, 68 cases have been registered through a national investigation. BSS-associated bleeding symptoms, such as skin ecchymosis, epistaxis, and gingival bleeding, are caused by platelet reduction and dysfunction and they usually present in early childhood; more severe episodes are associated with surgical procedures, dental extractions, menses, and accident[2]. We report hemostasis management and tooth extraction in a patient with severe BSS-related bleeding.

CASE REPORT

A 40-year-old male underwent extraction of the second left maxillary molar while receiving platelet transfusion. He had repeated nosebleeds from 1 year of age and had been diagnosed with idiopathic thrombocytopenic purpura (ITP) because of thrombocytopenia (bone marrow megakaryocytes were in the normal range) and had received whole blood or platelet concentrate transfusions for hemostasis. He was diagnosed with BSS at 17 years of age via evaluation of blood smears containing giant platelets and a biochemical flow cytometric platelet surface assessment that revealed a defective platelet membrane GPIb-X-V complex. His parents and sons had no bleeding histories, but his parents had a consanguineous marriage. His previous history was as follows: at 7 years of age, he suffered from epilepsy and began using phenobarbital. At 14 years of age, his epileptic symptoms disappeared and he stopped treatment. At 25 years of age, he was diagnosed with chronic hepatitis C consequent to frequent blood transfusion during childhood. At 39 years of age, he had cerebral hemorrhage

and required transfusion of 90 platelet units [platelet concentrate, 10 units; human leukocyte antigen (HLA)-matched platelets, 40 units, and cross-matching HLA-matched platelets, 40 units] as conservative therapy.

He had an average built with good nourishment. The skin and oral mucosa revealed no ecchymosis or petechiae. An oral examination revealed poor hygiene with redness and swelling of the maxillary and mandibular gingiva and dental calculus on most teeth. Blood clots were observed around the second right maxillary premolar (Fig 1-a). The second left maxillary molar was cracked and decayed to the dental pulp (Fig 1-b). The preoperative platelet count was abnormally low (7×10^9/L), measured using the automated hematology analyzer XN-9000 (Sysmex, Kobe, Japan) with the impedance measuring method in the whole-blood mode. This low platelet count was automatically converted and measured via the optics method in the fluorescent platelet channel (PLT-F) for a value of 17×10^9/L. Normal blood coagulability was evidenced from the following: prothrombin time, 11.4 s; international normalized ratio, 0.93; and activated partial thromboplastin time, 28.5 s. The liver function was slightly deteriorated as indicated by the following: aspartate aminotransferase, 36 U/L; alanine aminotransferase, 61 U/L; and gamma glutamyl transferase, 71 U/L.

Giant platelets were detected in the pathological blood smear; these platelets were slightly larger than red blood cells (Fig. 2). In a biochemical assessment, the reduced levels of platelet membrane glycoproteins GPIX and GPIbα were detected via flow cytometry.

In October 2013, the second left maxillary molar was extracted with platelet transfusion. To prevent an allergic reaction, we administered hydrocortisone before extracting the patient's left maxillary molar while transfusing 10 units of HLA-matched platelets. The tooth was

removed surgically, and little bleeding was observed. The extraction sites were packed with gelatine sponges and a splint was used for hemostasis (Fig 3-a,b). The postoperative PLT-F count increased to an estimated 37 × 10^9/L. Further examination revealed deficient ristocetin-induced platelet aggregation before and after transfusion (Table 1). Three days after extraction, we removed the extraction site hematoma under local anaesthesia and adjusted the splint, which did not fit the extraction sites because of the hematoma (Fig 3-c). Seven days after extraction, continuous bleeding from the palatal side of the gingival margin and an infection of the buccal side of the gingival margin were identified at the extraction site. We initiated carbazochrome sodium sulfonate hydrate and tranexamic acid treatment along with antibiotics. Eleven days later, secondary healing was achieved at the extraction site with no bleeding, indicative of excellent hemostasis.

DISCUSSION

Congenital platelet disorders related to adhesion, activation, secretion, aggregation or number are often indistinguishable from various coagulopathies solely according to clinical manifestations[2]. As in our patient, BSS —a congenital platelet disorder—is frequently misdiagnosed as ITP because of the prolonged bleeding time and thrombocytopenia and often is treated unsuccessfully with steroids or splenectomy. BSS-associated bleeding usually presents as minor symptoms such as epistaxis and frequent gingival bleeding; potential fatality due to bleeding (e.g., cerebral bleeding) is very rare[3]; however, our case was among these rare cases. BSS-associated bleeding is considered to be caused by qualitative or quantitative defects or reductions in the platelet membrane GPIb-X-V complex, a primary platelet adhesion receptor [1, 4]. Our patient was diagnosed with BSS after a flow cytometric biochemical platelet assessment to detect the platelet membrane GPIb-X-V complex.

In this case, the appearance of giant platelets in the pathological blood smear examination

confirmed the diagnosis; these platelets may be excluded from impedance counts, thus yielding falsely low values. Accordingly, platelets in such cases are counted via visual microscopic evaluation.

Recent attention has been given to an available automatic optics measurement method in PLT-F. This method performs hematological analyses via flow cytometry with a semiconductor laser. Platelets are analyzed in a two-dimensional scattergram in which the X-axis represents the intensity of the side-scattered fluorescent light (SFL) and the Y-axis represents the intensity of the forward-scattered light (FSC). SFL provides information on the degree of blood cell staining, whereas FSC provides information on the blood cell size (Fig. 4). In our case, we measured the patient's platelet count using an automated hematology analyzer (XN-9000) with an automatic retesting function. Impedance measurement yielded a preoperative platelet count of 7×10^9/L, whereas the optics method yielded a value of 17×10^9/L; given this increase, the giant platelet count was estimated as 1×10^9/L. The optical platelet count correlated strongly with the reference flow cytometric method, particularly at platelet counts of $<100 \times 10^9$/L. At this level, the optics method is far more reliable than impedance counting and will thus facilitate more appropriate clinical decisions, particularly with regard to platelet transfusion[5]. This system also improves workflow efficiency and confidence in abnormal sample results in routine hematology laboratories[6].

Many factors affect bleeding time reproducibility. The results are highly operator-dependent, with significant inter-operator variability[7]. Normal skin bleeding times range from 1 to 3 min; however, skin bleeding times have been found to be inaccurate and non-reproducible. In our case, this time was marginally prolonged to 5 min before transfusion. We expected time reduction after transfusion but instead observed an increase to 7 min. Therefore, the bleeding

times were not consistent with the clinical bleeding symptoms. This suggests difficulty in diagnosing hematologic diseases from only the skin bleeding time. Platelet aggregation tests were considered valuable for the differential diagnosis of congenital platelet disorders. However, the results of such examinations vary because of the blood collection and platelet-rich plasma techniques, interval from blood collection to examination, and inducer stability. Therefore, re-examination of abnormal values is required for confirmation[8].

Hemostasis or prophylaxis for bleeding prevention during surgical procedures usually requires transfusion of blood and/or platelets, despite the risk that the patients will develop antiplatelet and/or anti-erythrocyte alloantibodies[2,9]. We should therefore minimize platelet transfusion because antiplatelet reactions are known to reduce the effects of hemostasis. In our case, chronic hepatitis C and previous intracerebral hemorrhage aggravated the bleeding tendency. We expected postprocedural hemostatic difficulties due to severe thrombocytopenia and platelet dysfunction. The patient had received HLA-matched platelet transfusions to treat intracerebral hemorrhage. Consequently, we prepared the same HLA-matched platelets when planning platelet transfusion. Using antifibrinolytic drugs such as ε-aminocaproic acid or tranexamic acid may or may not be beneficial. The different responses of individual patients to these latter measures may reflect differences in the underlying disease; those with milder forms are more likely to respond to these therapies[2]. In our case, little postprocedural bleeding continued for some days. We avoided additional postoperative HLA-matched platelet transfusion using a splint and by administering carbazochrome sodium sulfonate hydrate and tranexamic acid.

There have been some reports regarding the perioperative management of patients with BSS in oral and maxillofacial surgery. Hartman et al[9] presented a patient with BSS who

underwent third molar extractions; treatment with preoperative and intraoperative systemic aminocaproic acid, seven HLA-matched platelet units, and topical gelfoam and thrombin resulted in sustained hemostasis and a durable healing response. Yoshiga et al[10] presented a patient with BSS who underwent ameloblastoma enucleation under general anesthesia; intravenous hydrocortisone administration prevented an allergic reaction to transfusion, which was initiated platelet transfusion. Total 15 HLA-matched platelet units were administered to avoid alloimmunization. The operation was completed without abnormal bleeding, and the postoperative course was good without bleeding[10].

In conclusion, we extracted a tooth and transfused overall 10 HLA-matched platelet units, using gelatine sponges and a splint for hemostasis. Frequent platelet transfusion makes antibodies that correspond to HLA on platelets. It is known that increase in the number of antibodies to transfused platelets causes reduction in hemostatic effect. In this case, we prepared HLA-matched platelets. Persistent bleeding from the extraction sites was recognized and treated with carbazochrome sodium sulfonate hydrate and tranexamic acid along with antibiotics. Accordingly, we avoided additional postoperative platelet transfusion and achieved wound healing.

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Legends

Fig. 1-a

An oral examination revealed poor hygiene with redness and swelling of the maxillary and mandibular gingiva and dental calculus on most teeth. Blood clots were observed around the second right maxillary premolar.

Fig. 1-b

The second left maxillary molar was cracked and decayed to the dental pulp.

Fig. 2

Microscopic view of the peripheral blood smear. Giant platelets were detected; these platelets were slightly larger than red blood cells.

Fig. 3-a

The extraction sites were packed with gelatine sponges.

Fig. 3-b

Used splint for hemostasis.

Fig. 3-c

Three days after extraction. Continuous bleeding from the palatal side of the gingival margin and an infection of the buccal side of the gingival margin were identified at the extraction site.

Fig. 4

Flow cytometric analysis of platelets. Histograms present control platelets and those collected from the patient before and after transfusion (A). The peak value for the control was approximately 8 fL; those for the patient before and after transfusion were approximately 30–40 fL (▼). This indicates that the patient's samples contained many giant platelets. A post-transfusion sample exhibited an increase at approximately 8–10 fL, indicating the addition of normal platelets from the transfusion (▼). A scattergram shows the control platelets and those from the patient before and after transfusion (B). These data indicate that

the platelet size convergence was smaller for the control than for the patient (▼)

Table 1

Result of platelet examinations and blood coagulation tests.

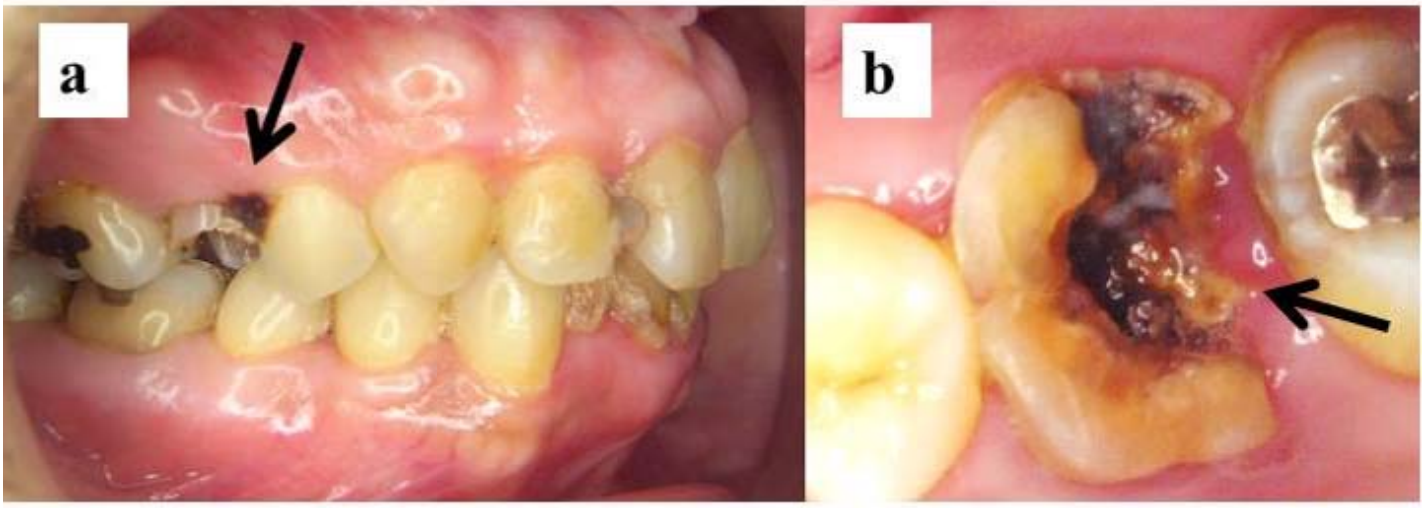

Fig. 1 Intraoral photograph at the initial examination

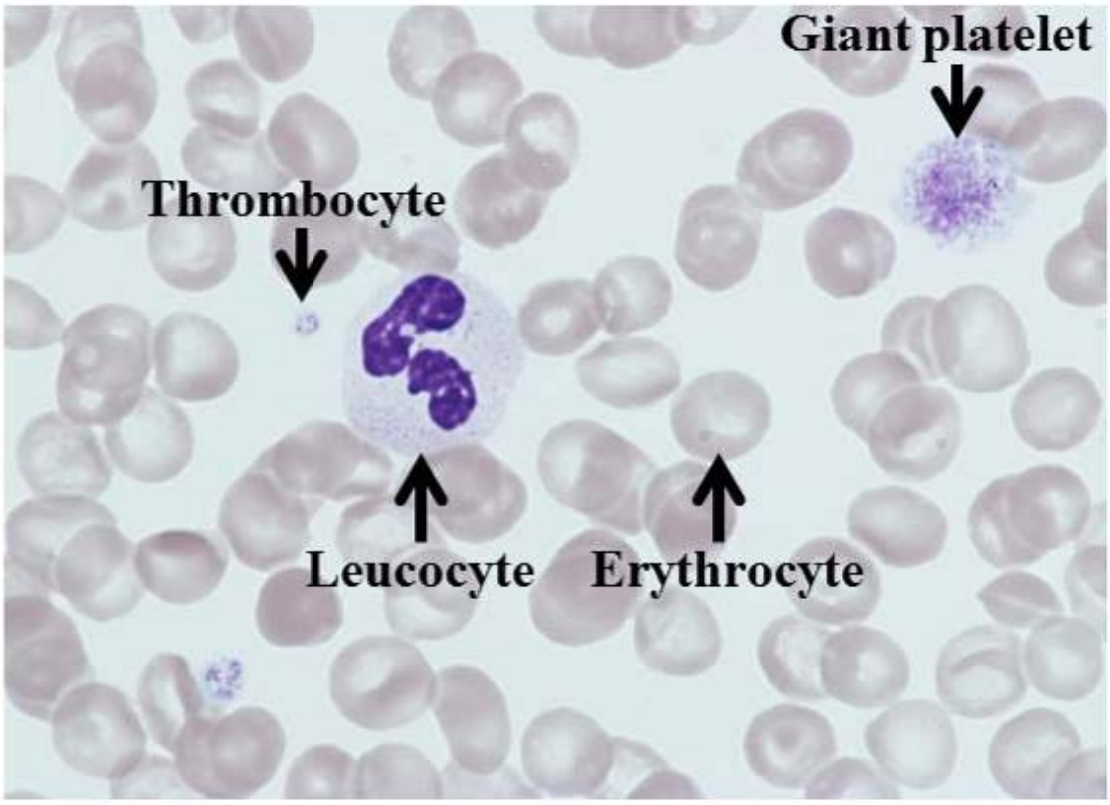

Fig. 2 Microscopic view of the peripheral blood smear.

Fig. 3 Photograph of extracion sites and splint

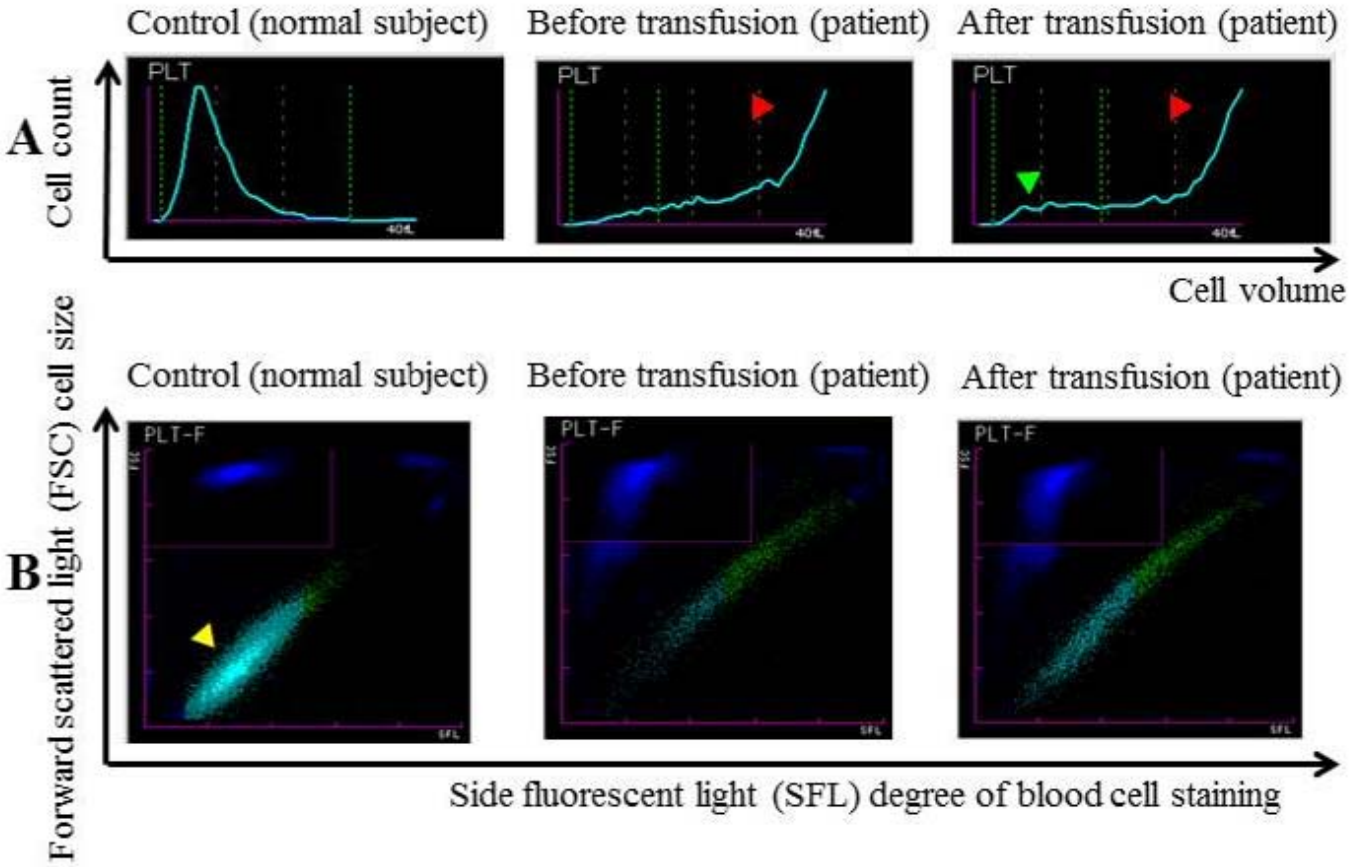

Fig. 4 Flow cytometric analysis of platelets.

Table 1 Laboratory date

	tooth extraction day		3 days after tooth extraction	7 days after tooth extraction
	Before platelet transfusion	After platelet transfusion		
Platelet count ($\times 10^9$/L) impedance method	7	29	8	9
Platelet count ($\times 10^9$/L) optics method	17	37	25	31
[a]PT (%)	129	99	79	92
PT (s)	11.4	12.1	13.2	12.4
PT [b](INR)	0.93	1.01	1.10	1.03
[c]APTT (s)	28.5	29.4	32.0	29.3

Aggregation with ristocetin	↓	↓	-	-
Skin bleeding time (min)	5	7.8	-	-
[d]FIB (mg/dl)	230	-	281	-
Thrombotest (%)	181	-	116	-

[a] PT, prothrombin time

[b] INR, international normalized ratio

[c] APTT, activated partial thromboplastin time

[d] FIB, fibrinogen